

ABSTRACT

Title

Role of serum ADAMTS13 and von Willebrand Factor (VWF) as early prognostic markers in identifying the disease course in Dengue fever.

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Background

Dengue is one of the common illnesses affecting children at Vellore and all over India. A significant proportion of children with dengue fever develop severe dengue including dengue hemorrhagic fever and dengue shock syndrome. Although most cases of severe illness are characterized by plasma leakage, thrombocytopenia and bleeding, the exact pathophysiology is not yet known. There are various proposed theories for causation of severe dengue. The recent evidence shown that in dengue patients there is an acquired deficiency of ADAMTS13 which causes high levels of VWF and subsequently consumptive coagulopathy.

This prospective study aims to identify those patients with dengue fever who will progress to severe disease by studying whether levels of two important biomarkers of

endothelial cell activation/ dysfunction, viz. VWF and ADAMTS 13 during early illness are predictive of progression to severe dengue and consequent morbidity and mortality.

Objectives

To ascertain the role of ADAMTS13 deficiency and von Willebrand Factor (VWF) excess as early markers in identification of risk of progression to severe dengue in patients with Dengue fever

Methods

Prospective study correlating levels of ADAMTS13 and VWF among children with dengue during the early febrile phase (day 1-4) with clinical severity and laboratory parameters of severe disease.

Results

ADAMTS13 levels were deficient in 96% of study children, irrespective of stage or phase of dengue infection. Von Willebrand Factor (VWF) activity by collagen-binding assay (CBA) was elevated in 89% of children with dengue infection. VWF activity was elevated in severe dengue compared to non-severe dengue, and in the early toxic phase compared to the febrile phase in children with severe dengue. Neither ADAMTS13 nor VWF activity levels were predictive of the WHO clinical stage of severity of dengue infection in our children.

Among clinical markers of severity of illness, hepatomegaly, ascites and pleural effusion, bleeding manifestations, need for blood and inotropic support and total duration of hospital stay were all significantly higher in children with severe dengue.

Hepatomegaly at admission and need for ICU admission were seen in children with higher median VWF levels. Need for blood support was significantly associated with lower ADAMTS13 levels.

Conclusions

Markers of endothelial injury such as low ADAMTS13 activity and elevated VWF activity are present in all stages and phases of infection in children with dengue. The median levels of ADAMTS13 and VWF activity did not correlate with either the WHO stages of the disease or the phases of the illness, and therefore cannot be used as prognostic biomarkers of severity of illness due to dengue.

Key words: ADAMTS13, VWF, DENGUE